REMARKS

In the Office Action dated January 8, 2008, claims 1-5, 8, 11-14, 18, 22, 29-32 and 36 are pending. The Examiner has made the restriction requirement final. As such, claims 1-5, 8, 11-14, and 18 are under examination. Claims 22, 29-32, and 36 are withdrawn from further consideration as directed to non-elected embodiments. The disclosure is objected to for certain informalities. The title is also objected to as not descriptive. Claims 11-14 are objected to for inconsistencies in the claim language. Claims 1 and 18 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. Claims 1-3, 5, and 8 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent No. 5,449,515 to Hamilton et al. Claims 1-5, 8, and 11-14 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent Appln. Publication 20070059280 ("the '280 publication") by Devalaraja et al., as evidenced by Luross et al. (*Immunology 103(4)*: 407-416, 2001).

This Response addresses each of the Examiner's objections and rejections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Formality Objections

The specification is objected to for certain informalities. The Examiner states that the last paragraph of page 32 is illegible, and requests Applicants to provide a legible copy of this paragraph.

In response, Applicants reproduce the last paragraph of page 32 here:

> "The genetically modified animals may also produce larger amounts of G-CSF or G-CSFR. For example, over expression of normal G-CSF or G-CSFR may produce dominant negative effects and may become useful disease models."

The title is objected to as not descriptive. Applicants have amended the title to read "A Method for Treatment and Prophylaxis of Arthritis by Inhibiting Activities of G-CSF and/or G-CSFR." Applicants respectfully submit that the new title is clearly descriptive of the invention to which the claims are directed.

In view of the foregoing, withdrawal of the objections to the specification and the title is respectfully requested.

Claim Objections

Claims 11-14 are objected to for inconsistencies in the claim language. The Examiner alleges that dependent claims 11-14 recite the term "antagonist", independent claim 1 does not recite the term "antagonist," but recite "an agent" which inhibits the activity or level of expression of..."

Applicants have canceled Claims 11 and 14 without prejudice. Applicants have amended Claims 12-13 to depend from Claim 1. Applicants have also amended Claim 1 to clarify the claim language. Support for the amendment to Claim 1 is found in Claims 11, 14 and 18 as previously presented. No new matter is introduced by the amendment to Claims 1 and 12-13. It is respectfully submit that the objection to Claims 11-14 is obviated in view of the foregoing amendments. Withdrawal of the objection is therefore respectfully requested.

35 U.S.C. §112, First Paragraph (Enablement) Rejection

Claims 1 and 18 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. The Examiner acknowledges that the specification provides enablement for a method of treating arthritis by administering a polypeptide or small molecule

agent which inhibits the activity or level of expression of G-CSF or G-CSFR. However, the Examiner alleges that the present invention does not provide enablement for a method of treating arthritis by administering an agent that is a DNA or RNA antagonist and contains a sense or antisense polynucleotide sequence or a generic sequence encoding G-CSF or G-CSFR. The Examiner contends that such nucleic acid-based administration reads on gene therapy and is not enabled by the specification.

Applicants have canceled Claim 18, without prejudice, and have amended Claim 1. Applicants reserve the right to file a continuation application to pursue the subject matter of Claims 1 and 18 as originally filed. Claim 1, as amended, is directed to a method based on administration of a polypeptide or antibody-based agent that inhibits the activity or level of expression of G-CSF or G-CSFR. It is respectfully submitted that the subject matter of claim 1, as presently claimed, is consistent with what the Examiner has acknowledged as enabled.

In view of the foregoing, the rejection under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support, is overcome. Withdrawal of the rejection is respectfully requested.

35 U.S.C. §102(b) Rejection

Claims 1-3, 5 and 8 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent No. 5,449,515 to Hamilton et al. The Examiner alleges that Claims 1-3, 5, and 8 recite a method of treatment of arthritis comprising administering to the subject an effective amount of an agent which inhibits the activity or level of expression of G-CSF or G-CSFR. The Examiner alleges that the '515 patent teaches a method of treating inflammatory disorders, including rheumatoid arthritis, comprising administering IL-4 for decreasing the production

(level of expression) of G-CSF.

Applicants observe that Claim 1, as presently recited, is directed to a method for the treatment of arthritis by administering an antibody to granulocyte-colony stimulating factor (G-CSF), an antibody to granulocyte-colony stimulating factor receptor (G-CSFR), soluble G-CSFR, or a G-CSF-binding fragment of the G-CSFR. Applicants respectfully submit that the '515 patent does not disclose the method of Claim 1, as amended, or the subject matter of Claims 3, 5 and 8, which claims depend from Claim 1.

Therefore, the rejection of Claims 1-3, 5 and 8 under 35 U.S.C. §102(b) as allegedly anticipated by the '515 patent is overcome and withdrawal thereof is respectfully requested.

35 U.S.C. §102(e) Rejection

Claims 1-5, 8 and 11-14 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent Appln. Publication 20070059280 ('the '280 publication") by Devalaraja et al., as evidenced by Luross et al. (*Immunology* 103(4): 407-416, 2001).

The Examiner alleges that the '280 publication teaches a method of treating inflammation or an autoimmune disease by administering to a mammal in need thereof a therapeutically effective amount of an inhibitor of a G-CSF, which inhibits inflammation or autoimmune disease. The '280 publication also allegedly teaches that inhibitors of G-CSF and G-CSFR include antibodies. Further, the '280 publication allegedly teaches administration of anti-G-CSF antibodies to a human, as well as administration of soluble G-CSFRs, which prevent interaction with naturally-occurring receptors. Moreover, according to the Examiner, "[t]he '280 publication defines autoimmune diseases to include those with anti-collagen antibodies, thereby

encompassing collagen-induced arthritis." By referencing Luross et al., the Examiner further alleges that it is well-known in the art that collagen-induced arthritis is an animal model of human rheumatoid arthritis. Thus, the Examiner alleges that the '280 publication anticipates the instant methods.

In response, Applicants respectfully submit that the '280 publication does not provides adequate teaching sufficient to anticipate the claimed invention. In the first instance, Applicants observe that the alleged therapeutic methods disclosed in the '280 publication are merely based on an observation of the synergistic effect of exogenously added G-CSF on chemokine-mediated inflammation. For example, the '280 publication discloses intradermal recruitment of neutrophils by G-CSF plus IL-8, both injected intradermally (see Figure 5 and paragraph 0129). Additionally, the '280 publication discloses the potentiating effect of G-CSF on IL-8-mediated chemotaxis (see Figures 7 and 8. Again, in these experiments, both G-CSF and IL-8 were added to the assays (see paragraph [0128]). Essentially based solely on such synergistic effect of G-CSF on chemokine-mediated inflammation, and absent any evidence with respect to the role of endogenously produced G-CSF in inflammation, the '280 publication "proposed" that administration of an inhibitor of CSF would be "a useful tool" (see paragraph 0134). Applicants respectfully submit that the evidence provided in the '280 publication, showing a positive effect of exogenous G-CSF on a cytokine, simply does not adequately support a therapeutic method of treating a disease based on inhibiting (i.e., negating) endogenous G-CSF.

In contrast, the present application demonstrates that G-CSF alone has the effect of driving bone marrow leukocyte production during inflammatory diseases, such as rheumatoid arthritis. See, e.g., page 40-41 of the specification. The present application provides direct evidence for a role of endogenously produced G-CSF in promoting inflammation *in vivo*, by

using G-CSF gene knockout mice in collagen induced arthritis (see Example 14, page 42 of the present specification), which is the most widely accepted mouse model of this human disease. The present application also provides direct evidence that bone marrow production of myeloid cells is enhanced during arthritis and that this response is markedly reduced in G-CSF gene knockout mice.

The '280 publication, on the other hand, does not provide any showing based on an accepted experimental model of arthritis. Moreover, the '280 publication does not provide any evidence with respect to a therapeutic effect against the progression of a relevant experimental model of inflammation or arthritis.

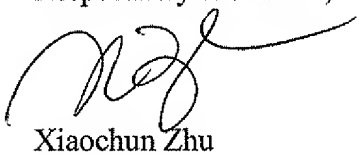
Distinguishing from the '280 publication, the present application provides direct evidence showing that specific blockade of G-CSF in wild type mice by administration of anti-G-CSF antibodies prior to and after the induction of acute arthritis provides a protective effect against the development and progression of disease. See, e.g., page 45, Example 20, and Figures 14A-D of the present application.

Accordingly, considering the entirety of the disclosure in the '280 publication, Applicants respectfully submit that the '280 publication does not provide adequate teaching with respect to treating an inflammatory disease based on administration of an inhibitor of CSF, or more specifically respecting treating arthritis by administering an antibody against G-CSF, a soluble G-CSFR or a fragment thereof, as presently claimed. The prior art must be enabling to anticipate. Preemption Devices Inc. v. Minnesota Mining & Mfg. Co., 732 F.2d 903, 906, 221 U.S.P.Q. (BNA) 841, 843 (Fed. Cir. 1984). The '280 publication simply lacks enabling disclosure with respect to a method of treating arthritis by administering an antibody against G-CSF, a soluble G-CSFR or a fragment thereof, as presently claimed.

Accordingly, Applicants respectfully submit that the '280 publication does not anticipate the presently claimed invention. Therefore, the rejection of Claims 1-5, 8, and 11-14 under 35 U.S.C. §102(e) based on the '280 publication is overcome and withdrawal thereof is respectfully requested.

In view of the foregoing amendments and remarks, it is firmly believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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